

FIG. 1A

ttatgcaaga aactgttgaa ttagaccctgt ttcctataga tgagaaacca tacaagctgt  
 ggtatztatg agcctccatt tcttatacta ctgcagtga ccaacattgg atgtgaaaat  
 tgccttttgt cagggattcg ataaacaagt ggatgtgtca tatattgcca aacattacaa  
 catgagcaaa agcaaagttg acaaccagtt ctacagtgtg gaagtgggag actcaacctt  
 cacagttctc aagcgctacc agaactaaa gcctattggc tctggggctc agggcatagt  
 ttgtgccgcg tatgatgctg tccttgacag aaatgtggcc attaagaagc tcagcagacc  
 ctttcagaac caaacacatg ccaagagagc gtaccgggag ctggtcctca tgaagtgtgt  
 gaaccataaa aacattatta gtttattaaa tgtcttcaca cccagaaaa cgctggagga  
 gttccaagat gtttacttag taatggaact gatggatgcc aacttatgtc aagtgattca  
 gatggaatta gaccatgagc gaatgtctta cctgctgtac caaatgttgt gtggcattaa  
 gcacctccat tctgctggaa ttattcacag ggatttaaaa ccaagtaaca ttgtagtcaa  
 gtctgattgc acattgaaaa tcctggactt tggactggcc aggacagcag gcacaagctt  
 catgatgact ccatatgtgg tgacacgtta ttacagagcc cctgagggtca tcctggggat  
 gggctacaag gagaacgtgg atatatggtc tgtgggatgc attatgggag aaatgggttcg  
 ccacaaaatc ctctttccag gaagggacta tattgaccag tggataaagg taattgaaca  
 actaggaaca ccatgtccag aattcatgaa gaaattgcaa cccacagtaa gaaactatgt  
 ggagaatcgg cccaagtatg cgggactcac cttcccaaaa ctcttcccag attcctctct  
 cccagcggac tccgagcaca ataaactcaa agccagccaa gccagggact tgttgtcaaa  
 gatgctagtg attgaccag caaaaagaat atcagtggac gacgccttac agcatcccta  
 catcaacgtc tggatgacc cagccgaagt ggaggcgcct ccacctcaga tatatgacaa  
 gcagttggat gaaagagaac acacaattga agaattgaaa gaacttatct acaaggaagt  
 aatgaattca gaagaaaaga ctaaaaatgg tgtagtaaaa ggacagcctt ctcttcagg  
 tgcagcagtg aacagcagtg agagtctccc tccatcctcg tctgtcaatg acatctctc  
 catgtccacc gaccagaccc tggcatctga cactgacagc agcctggaag cctcggcagg  
 acccctgggt tgttgaggt gactagccgc ctgcctgcga aaccagcgt tcttcaggag  
 atgat (SEQ ID NO:1)

FIG. 1B

MSLHFLYYCSEPTLDVKIAFCQGFQVDVSYIAKHYNMSKSKVDNQFYSEVGDSTFTVL  
KRYQNLKPIGSGAQGIVCAAYDAVLDRNVAIKKLSRPFQNTAKRAYRELVLKCVNHKN  
IISLLNVFTFPQKTLEEFQDVYLVMEMLDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSA  
GIIHRDLKPSNIVVKSCTLKILDFGLARTAGTSFMMTPYVVTRYRAPEVILGMGYKENV  
DIWSVGCIMGEMVRHKILFPGRDYIDQWNKVIEQLGTPCPEFMKKLQPTVRNYVENRKYA  
GLTFPKLFPDSLFPADSEHNKLKASQARDLLSKMLVIDPAKRISVDDALQHPYINVWYDPA  
EVEAPPPQIYDKQLDEREHTIEEWKELIYKEVMNSEKTKNGVVKGQPSPSGAAVNSSESL  
PPSSSVNDISSMSTDQTLASDTDSLEASAGPLGCCR (SEQ ID NO: 2)

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FIG. 1C

GAGAAATGGCGTGGCAGGGGACCCAGCGAGCCCAGAGGGATTTTGCCGCTGCTTCCTCTAC  
CCCTGTATTTTACGCAGCTCTCTAAATTGACTCAGCTCCAGGCTAGTGTGAGAAACACCAA  
CAGCAGGCCCATCTCAGATCTTCACTATGGCAACTTATGCAAGAACTGTTGAATTAGACC  
CGTTTCCTATAGATGAGAAACCATAACAAGCTGTGGTATTTATGAGCCTCCATTTCTTATAC  
TACTGCAGTGAACCAACATTGGATGTGAAAATTGCCTTTTGTGAGGGATTGATAAACAAAG  
TGGATGTGTCATATATTGCCAAACATTACAACATGAGCAAAAGCAAAGTTGACAACCAGTT  
CTACAGTGTGGAAGTGGGAGACTCAACCTTTCAGATTCTCAAGCGCTACCAGAATCTAAAG  
CCTATTGGCTCTGGGGCTCAGGGCATAGTTTGTGCCGCGTATGATGCTGTCCTTGACAGAA  
ATGTGGCCATTAAGAAGCTCAGCAGACCCTTTCAGAACCAAACACATGCCAAGAGAGCGTA  
CCGGGAGCTGGTCTCATGAAGTGTGTGAACCATAAAAAACATTATTAGTTTATTAAATGTC  
TTCACACCCCAGAAAACGCTGGAGGAGTTCCAAGATGTTTACTTAGTAATGGAAGTATGG  
ATGCCAACTTATGTCAAGTGATTGAGATGGAATTAGACCATGAGCGAATGTCTTACCTGCT  
GTACCAAATGTTGTGTGGCATTAAAGCACCTCCATTCTGCTGGAATTATTACAGGGATTTA  
AAACCAAGTAACATTGTAGTCAAGTCTGATTGCACATTGAAAATCCTGGACTTTGGACTGG  
CCAGGACAGCAGGCACAAGCTTCATGATGACTCCATATGTGGTGACACGTTATTACAGAGC  
CCCTGAGGTCATCCTGGGGATGGGGCTACAAGGAGAACGTGGATATATGGTCTGTGGGATGC  
ATTATGGGAGAAATGGTTCGCCACAAAATCCTCTTTCAGGAAGGGACTATATTGACCACT  
GGAATAAGGTAATTGAACAACCTAGGAACACCATGTCCAGAATTCATGAAGAAATTGCAACC  
CACAGTAAGAACTATGTGGAGAATCGGCCCAAGTATGCGGGACTCACCTTCCCCAACTC  
TTCCCAGATTCCCTCTTCCCAGCGGACTCCGAGCACATAAACTCAAAGCCAGCCAAGCCA  
GGGACTTGTTGTCAAAGATGCTAGTGATTGACCCAGCAAAAAGAATATCAGTGGACGACGC  
CTTACAGCATCCCTACATCAACGTCTGGTATGACCCAGCCGAAGTGGAGGCGCTCCACCT  
CAGATATATGACAAGCAGTTGGATGAAAGAGAACACACAATTGAAGAATGGAAAGAACTTA  
TCTACAAGGAAGTAATGAATTGAGAAGAAAAGACTAAAAATGGTGTAGTAAAAGGACAGCC  
TTCTCCTTCAGGTGCAGCAGTGAACAGCAGTGAGAGTCTCCCTCCATCCTCGTCTGTCAAT  
GACATCTCCTCCATGTCCACCGACCAGACCCTGGCATCTGACACTGACAGCAGCCTGGAAG  
CCTCGGCAGGACCCCTGGGTTGTTGCAGGTGACTAGCCGCTGCCTGCGAAACCCAGCGTT  
CTTCAGGAGATGATGTGATGGAACACACACACACGACACACACACACACAAATGCA  
GACACACAACATCAAGAAAACAGCAAGGGAGAGAATCCAAGCCTAAAATTAAATAAATCTT  
TCAGCCTGCTTCTTCCCCAGGGTCTGTATTGCAGCTAAGCTCAAATGTATATTTAACTTC  
TAGTTGCTCTTGCTTTGGTCTTCTTCCAATGATGCTTACTACAGAAAGCAAATCAGACACA  
ATTAGAGAAGCCTTTTCCATAAAGTGTAATTTTAATGGCTGCAAAACCGGCAACCTGTAAC  
TGCCCTTTTAAATGGCATGACAAGGTGTGAGTGGCCCCATCCAGCATGTGTGTGTCTCTA  
TCTTGCATCTACCTGCTCCTTGGCCTAGTCAGATGGATGTAGATACAGATCCGCATGTGTC  
TGTATTTCATACAGCACTACTTACTTAGAGATGCTACTCTCAGTGTCTCAGGGCTCTACCA  
AGACATAATGCACTGGGGTACCACATGGTCCATTTTCATGTGATCTATTACTCTGACATAAA  
CCCATCTGTAATATATTGCCAGTATATAAGCTGTTTGTAGTTTGTAAATTGATTAACTGTAT  
GTCTTATAAGAAAACATGTAAAGGGGGAATATATTGGGGGAGTGAGCTCTCTCAGACCCTT  
GAAGATGTAGCTTCCAAATTTGAATGGATTAAATGGCACCTGTATACCA (SEQ ID NO:3)

GAGAAATGGCGTGGCAGGGGACCCAGCGAGCCCAGAGGGATTTTGCCGCTGCTTCCTCTAC

FIG. 2A

atctcagatc ttactatgg caacttatgc aagaaactgt tgaattagac ccgtttccta  
 tagatgagaa accatacaag ctgtggtatt tatgagcctc ctttcttataactactgcag  
 tgaaccaaca ttggatgtga aaattgcctt ttgtcaggga ttcgataaac aagtggatgt  
 gtcatatatt gccaaacatt acaacatgag caaaagcaaa gttgacaacc agttctacag  
 tgtggaagtg ggagactcaa ccttcacagt tctcaagcgc taccagaatc taaagcctat  
 tggctctggg gctcagggca tagtttgtgc cgcgtatgat gctgtccttg acagaaatgt  
 ggccattaag aagctcagca gaccctttca gaaccaaaaca catgccaaga gagcgtaccg  
 ggagctggtc ctcatgaagt gtgtgaacca taaaaacatt attagtttat taaatgtctt  
 cacaccccag aaaacgctgg aggagttcca agatgtttac ttagtaatgg aactgatgga  
 tgccaactta tgtcaagtga ttcagatgga attagaccat gagcgaatgt cttacctgct  
 gtaccaaagt ttgtgtggca ttaagcacct ccattctgct ggaattattc acagggattt  
 aaaaccaagt aacattgtag tcaagtctga ttgcacattg aaaatcctgg actttggact  
 ggccaggaca gcaggcacia gcttcatgat gactccatat gtggtgacac gttattacag  
 agcccctgag gtcacccctgg ggatgggcta caaggagaac gtggatatat ggtctgtggg  
 atgcattatg ggagaaatgg ttcgccacia aatcctcttt ccaggaaggg actatattga  
 ccagtggaat aaggtaattg aacaactagg aacaccatgt ccagaattca tgaagaaatt  
 gcaaccaca gtaagaaact atgtggagaa tcggcccaag tatgcgggac tcacctccc  
 caaactcttc ccagattccc tcttcccagc ggactccgag cacaataaac tcaaagccag  
 ccaagccagg gacttgttgt caaagatgct agtgattgac ccagcaaaaa gaatatcagt  
 ggacgacgcc ttacagcatc cctacatcaa cgtctggtat gaccagccg aagtggaggc  
 gcctccacctcagatatatg acaagcagtt ggatgaaaga gaacacacia ttgaagaatg  
 gaaagaactt atctacaagg aagtaatgaa ttcagaagaa aagactaaaa atggtgtagt  
 aaaaggacag cttctcctt cagcacaggt gcagcagtga acagcagtga gagtctcct  
 ccatcctcgt ctgtcaatga catctcctcc atgtccaccg accagaccct ggcatctgac  
 actgacagca gcctggaagc ctcggcagga cccctgggtt gttgcagggt actagccgcc  
 tgcttgcgaa acccagcgtt cttcaggaga tgatgtgatg gaacacacac acacgcagac  
 acacacacac acacaaatgc agacacacia catcaagaaa acagcaaggg agagaatcca

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agcctaaaat taaataaatc tttcagcctg cttcttcccc aggggttctgt attgcagcta  
agctcaaatzg tatatttaac ttctagttgc tcttgctttg gtcttcttcc aatgatgctt  
actacagaaa gcaaattcaga cacaattaga gaa. (SEQ ID NO:4)

[illegible]

FIG. 2C

MSLHFLYYCSEPTLDVKIAFCQGFDKQVDVSYIAKHYNMSKSKVDNQFY SVEVG DSTFTVL  
KRYQNLKPIGSGAQGIVCAA YDAVLDRNVAIKKLSRPFQNT HAKRAYREL VLMKCVNHKN  
IISLLNVFTPQKTLEEFQDVYLVME LMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSA  
GIIHRDLKPSNIVVKSDCTLKILDFGLARTAGTSFMMTPYVVTRY YRAPEVILGMGYKENV  
DIWSVGCIMGEMVRHKILFPGRDYIDQWNKVIEQLGTPCPEFMKKLQPTVRNYVENRPKYA  
GLTFPKLFPDSLFPADSEHNKLKASQARDLLSKMLVIDPAKRISVDDALQHPYINVWYDPA  
EVEAPPPQIYDKQLDEREHTIEEWKELIYKEVMNSEEKTNGVVKGQPSPSAQVQQ (seq id no: 5)

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FIG. 2D

GAGAAATGGCGTGGCAGGGGACCCAGCGAGCCCAGAGGGATTTTGCCGCTGCTTCCTCTAC  
 CCCTGTATTTACGCAGCTCTCTAAATTGACTCAGCTCCAGGCTAGTGTGAGAAACACCAA  
 CAGCAGGCCCATCTCAGATCTTCACTATGGCAACTTATGCAAGAACTGTTGAATTAGACC  
 CGTTTCCTATAGATGAGAAACCATAAAGCTGTGGTATTTATGAGCCTCCATTTCTTATAC  
 TACTGCAGTGAACCAACATTGGATGTGAAAATTGCCTTTTGTGAGGGATTGATAAACAAAG  
 TGGATGTGTCATATATTGCCAAACATTACAACATGAGCAAAAGCAAAGTTGACAACCAGTT  
 CTACAGTGTGGAAGTGGGAGACTCAACCTTCACAGTTCTCAAGCGCTACCAGAATCTAAAG  
 CCTATTGGCTCTGGGGCTCAGGGCATAGTTTGTGCCGCGTATGATGCTGTCTTGACAGAA  
 ATGTGGCCATTAAGAAGCTCAGCAGACCCTTTCAGAACCAAACACATGCCAAGAGAGCGTA  
 CCGGGAGCTGGTCTCATGAAGTGTGTGAACCATAAAAACATTATTAGTTTATTAAATGTC  
 TTCACACCCCAGAAAACGCTGGAGGAGTTCCAAGATGTTTACTTAGTAATGGAAGTATGG  
 ATGCCAACTTATGTCAAGTGATTCAGATGGAATTAGACCATGAGCGAATGTCTTACCTGCT  
 GTACCAAATGTTGTGTGGCATTAAAGCACCTCCATTCTGCTGGAATTATTACAGGGGATTTA  
 AAACCAAGTAACATTGTAGTCAAGTCTGATTGCACATTGAAAATCCTGGACTTTGGACTGG  
 CCAGGACAGCAGGCACAAGCTTCATGATGACTCCATATGTGGTGACACGTTATTACAGAGC  
 CCCTGAGGTCATCCTGGGGATGGGCTACAAGGAGAACGTGGATATATGGTCTGTGGGATGC  
 ATTATGGGAGAAATGGTTTCGCCACAAAATCCTCTTTCAGGAAGGGACTATATTGACCAGT  
 GGAATAAGGTAATTGAACAACCTAGGAACACCATGTCCAGAATTCATGAAGAAATTGCAACC  
 CACAGTAAGAACTATGTGGAGAATCGGCCCAAGTATGCGGGACTCACCTTCCCCAACTC  
 TTCCCAGATTCCCTCTTCCCAGCGGACTCCGAGCACAATAAACTCAAAGCCAGCCAAGCCA  
 GGGACTTGTTGTCAAAGATGCTAGTGATTGACCCAGCAAAAAGAATATCAGTGGACGACGC  
 CTTACAGCATCCCTACATCAACGTCTGGTATGACCCAGCCGAAGTGGAGGCGCCTCCACCT  
 CAGATATATGACAAGCAGTTGGATGAAAGAGAACACACAATTGAAGAATGGAAAGAACTTA  
 TCTACAAGGAAGTAATGAATTCAGAAGAAAAGACTAAAAATGGTGTAGTAAAAGGACAGCC  
 TTCTCCTTCAGCACAGGTGCAGCAGTGAACAGCAGTGAGAGTCTCCCTCCATCCTCGTCTG  
 TCAATGACATCTCCTCCATGTCCACCGACCAGACCCTGGCATCTGACACTGACAGCAGCCT  
 GGAAGCCTCGGCAGGACCCCTGGGTTGTTGCAGGTGACTAGCCGCCTGCCTGCGAAACCCA  
 GCGTTCTTCAGGAGATGATGTGATGGAACACACACACACGACACACACACACACACAA  
 ATGCAGACACACAACATCAAGAAAACAGCAAGGGAGAGAATCCAAGCCTAAAATTAAATAA  
 ATCTTTCAGCCTGCTTCTTCCCCAGGGTTCTGTATTGCAGCTAAGCTCAAATGTATATTTA  
 ACTTCTAGTTGCTCTTGGTCTTCTTCCAATGATGCTTACTACAGAAAGCAAATCAG  
 ACACAATTAGAGAAGCCTTTTCCATAAAGTGTAATTTTAATGGCTGCAAAACCGGCAACCT  
 GTAAGTGCCTTTTAAATGGCATGACAAGGTGTGCAGTGGCCCCATCCAGCATGTGTGTGT  
 CTCTATCTTGCATCTACCTGCTCCTTGGCCTAGTCAGATGGATGTAGATACAGATCCGCAT  
 GTGTCTGTATTACATACAGCACTACTTACTTAGAGATGCTACTCTCAGTGTCTCAGGGCTC  
 TACCAAGACATAATGCACTGGGGTACCACATGGTCCATTTTCATGTGATCTATTACTCTGAC  
 ATAAACCCATCTGTAATATATTGCCAGTATATAAGCTGTTTGTGTTAATTGATTAAAC  
 TGTATGTCTTATAAGAAAACATGTAAAGGGGAATATATTGGGGGAGTGAGCTCTCTCAGA  
 CCCTTGAAGATGTAGCTTCCAAATTTGAATGGATTAAATGGCACCTGTATACCA (seq ID No: 6)

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gagaaatggc gtggcagggg acccagcgag cccagagggg ttttgccgct gcttcctcta  
 cccctgtatt tcacgcagct ctctaaattg actcagctcc aggctagtgt gagaaacacc  
 aacagcaggg ccattctcaga tcttcactat ggcaacttat gcaagaaact gttgaattag  
 acccgtttcc tatagatgag aaaccataca agctgtggta tttatgagcc tccatttctt  
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 acaagtggat gtgtcatata ttgccaaaca ttacaacatg agcaaaagca aagttgacaa  
 ccagttctac agtgtggaag tgggagactc aaccttcaca gttctcaagc gctaccagaa  
 tctaaagcct attggctctg gggctcaggg catagtttgt gccgcgtatg atgctgtcct  
 tgacagaaat gtggccatta agaagctcag cagacccttt cagaacccaa cacatgccaa  
 gagagcgtac cgggagctgg tcctcatgaa gtgtgtgaac cataaaaaca ttattagttt  
 attaaatgtc ttcacacccc agaaaacgct ggaggagtgc caagatgttt acttagtaat  
 ggaactgatg gatgccaaact tatgtcaagt gattcagatg gaattagacc atgagcgaat  
 gtcttacctg ctgtacccaa tgttgtgtgg cattaagcac ctccattctg ctggaattat  
 tcacagggat ttaaaaccaa gtaacattgt agtcaagtct gattgcacat tgaaaatcct  
 ggactttgga ctggccagga cagcaggcac aagcttcatg atgactccat atgtggtgac  
 acgttattac agagcccctg aggtcactct ggggatgggc tacaaggaga acgtggatat  
 atggtctgtg ggatgcatta tgggagaaat ggttcgccac aaaatcctct tccaggaag  
 ggactatatt gaccagtgga ataaggtaat tgaacaacta ggaacaccat gtccagaatt  
 catgaagaaa ttgcaacca cagtaagaaa ctatgtggag aatcggccca agtatgcggg  
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 actcaaagcc agccaagcca gggacttgtt gtcaaagatg ctagtgattg acccagcaaa  
 agaatatca gtggacgacg ccttacagca tccctacatc aacgtctggt atgaccagc  
 cgaagtggag gcgcctccac ctcatatata tgacaagcag ttggatgaaa gagaacacac  
 aattgaagaa tggaagaac ttatctacaa ggaagtaatg aattcagaag aaaagactaa  
 aatggtgta gtaaaaggac agccttctcc ttcagcacag gtgcagcagt gaacagcagt  
 gagagtctcc ctccatcctc gtctgtcaat gacatctcct ccattgtccac cgaccagacc

36207-22376



FIG. 3B

ctggcatctg acactgacag cagcctggaa gcctcggcag gacccctggg ttgttgacagg  
tgactagccg cctgcctgcg aaaccacagc ttcttcagga gatgatgtga tggaacacac  
acacacgcag acacacacac acacacaaat gcagacacac aacatcaaga aaacagcaag  
ggagagaatc caagcctaaa attaaataaa tctttcagcc tgcttcttcc ccagggttct  
gtattgcagc taagctcaaa tgtatattta acttctagtt gctcttgctt tggctcttct  
ccaatgatgc ttactacaga aagcaaatca gacacaatta gagaagcctt ttccataaag  
tgtaatttta atggctgcaa aaccggcaac ctgtaactgc ccttttaaat ggcatgacaa  
ggtgtgcagt ggcccatcc agcatgtgtg tgtctctatc ttgcatctac ctgctccttg  
gcctagtcag atggatgtag atacagatcc gcatgtgtct gtattcatac agcactactt  
acttagagat gctactctca gtgtcctcag ggctctacca agacataatg cactggggta  
ccacatggtc catttcatgt gatctattac tctgacataa acccatctgt aatatattgc  
cagtatataa gctgttttagt ttgttaattg attaaactgt atgtcttata agaaaacatg  
taaaggggga atatatggg ggagtgaact ctctcagacc cttgaagatg tagcttccaa  
atttgaatgg attaaatggc acctgtatac ca (SEQ ID NO: 7)

36203T 2255T 209

MSLHFLYYCSEPTLDVKIAFCQGFQVDVSYIAKHYNMSKSKVDNQFYSSVEVG DSTF  
TVLKRYQNLKPIGSGAQQIVCAAYDAVLDRNVAIKKLSRPFQNTAKRAYRELVL MK  
CVNHKNIISLLNVFTPQKTLEEFQDVYLVME LMDANLCQVIQMELDHERMSYLLYQML  
CGIKHLHSAGIIHRDLKPSNIVVKS DCTLKILDFGLARTAGTSFMMTPYVVTRYRAP  
EVILGMGYKENVDIWSVGCIMGEMVRHKILFPGRDYIDQWNKVIEQLGTPCPEFMKKL  
QPTVRNYVENRPKYAGLTFFPKLFPDSLFPADSEHNKLKASQARDLLSKMLVIDPAKRI  
SVDDALQHPYINVWYDPAEVEAPPPQIYDKQLDEREHTIEEWKELIYKEVMNSEKTK  
NGVVKGQPSPSAQVQQ (SEQ ID NO: 8)

363007-2233750

CCCTCCTTATTCCGGTTTGGAATGTGGCTAATGAAAGCCCAGTAGGAGGATTTCTGGGGCA  
AACAGGTGGACCAGGATCCTGGTTCTCAGGCACGGAATGGCTATTGTGAGAGCGCCACCAG  
CAGGACCATCGCAGATCTTGGTTATGGCTGCTCACGCAAGAGGCTGTTGATGTAGACCCCC  
TTTCCCGTAGATGAGAAATCACACGAGCAGTGGTATTTATGAGCCTCCATTTCTTATACTA  
CTGCAGTGAACCAACCTTGGATGTGAAAATTGCCTTTTGTTCAGGTGTGTGTTCCCTTACAGG  
TAAAACAAAGGGATTTCGACAAACACGTGGATGTGTCTTCTGTTGTCAAACATTACAACATG  
AGCAAAAGCAAGGTAGATAACCAGTTCTACAGTGTGGAAGTGGGAGACTCAACCTTCACAG  
TTCTAAAGCGCTACCAGAACCTGAAGCCGATCGGCTCTGGGGCTCAGGGAATAGTTTGTGC  
TGCGTATGACGCTGTCTCTCGACAGAAATGTGGCCATTAAGAAGCTCAGCAGACCCTTCCAG  
AACCAAACCTCATGCCAAGAGGGGCTTACCGGGAGCTGGTCCTCATGAAGTGTGTGAACCATA  
AAAACATTATTAGCTTATTAAATGTCTTTACACCCCAGAAAACACTGGAGGAGTTCGAAGA  
TGTTTACTTAGTGATGGAACCTGATGGACGCCAACTTGTGTTCAGGTGATTCAGATGGAGCTG  
GACCACGAGCGGATGTTCGTACTTGTGTACCAGATGCTGTTCGGCGATCAAACACCTCCACT  
CCGCTGGGATCATCCACAGGGACTTAAAACCCAGTAACATCGTAGTCAAGTCTGATTGCAC  
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TATGTGGTGACGAGATATTACAGAGCCCCGAGGTCATCCTGGGCATGGGCTACAAGGAGA  
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TCCCGGAAGGGACTATATTGACCAGTGGAACAAAGTCATAGAGCAGCTAGGAACTCCGTGT  
CCAGAATTCATGAAGAAATTGCAGCCCACCGTCAGAAACTACGTGGAGAACCGGCCCAAGT  
ATGCAGGCCTCACCTTCCCCAAGCTCTTTCAGATTCCCTCTTCCCAGCGGATTCCGAGCA  
CAATAAACTTAAAGCCAGCCAAGCCAGGGACTTGTTGTCAAAGATGTTAGTGATTGACCCA  
GCGAAGAGGATATCGGTGGATGACGCATTGCAGCATCCGTACATCAACGTTTGGTACGACC  
CTGCTGAAGTGGAGGCGCTCCGCCTCAGATATATGACAAGCAATTGGATGAAAGGGAGCA  
CACCATCGAAGAATGGAAAGAACTCATCTACAAGGAAGTAATGAACTCAGAAGAGAAGACT  
AAGAACGGCGTAGTCAAAGGCCAGCCCTCACCTTCAGGTGCAGCAGTGAACAGCAGTGAGA  
GTCTCCCTCCATCCTCATCTGTCAACGACATCTCCTCCATGTCCACCGACCAGACCCTCGC  
ATCCGACACTGACAGCAGCCTGGAAGCCTCGGCGGGACCGCTGGGTGTTGTTGCAGGTGACTA  
GCCGCCTGCCTGCGAAACCCAGCGTTCTTCAGGAGATGACGCCATGATAGAACACAGCGCA  
CATGCACACACACAGAGCTTGTAACACACACACACACACACACACGACGCACGCACG  
CACGCAAGCACGCACGCACGCACAAATGCACTCACGCAATGTCAAGAAAAAAAAAAGTAGC  
GAGAGAGAGCGAGAGAGCCAAACGTAAACTAAGTTAAATCTTTCTGCGTGCTTCTCCAGAG  
TTCTGTATCGCAGCTGAGCTGAAATGTATACTTAACCTTAGTCGCGCTCGCTCGACTTTG  
GTCTCCCTCCGGCAGTGCTTACT

(SEQ ID No: 9)

S520T:225T60

MSKSKVDNQFY SVEVG DSTFTVLKRYQNLKPIGSGAQGIVCAAYDAVLDRNVAIKKLSRPF  
QNQTHAKRAYRELVL MKCVNHKNIISLLNVFTPQKTLEEFQDVYLV MELMDANLCQVIQME  
LDHERMSYLLYQMLSAIKHLHSAGIIHRDLKPSNIVVKSDCTLKILDFGLARTAGTSFMMT  
PYVVTRY YRAPEVILG MGYKENVDIWSVGCIMGEMVRHKILFPGRDYIDQWNKVIEQLGTP  
CPEFMKKLQPTVRNYVENR PKYAGLTFFPKLFPDSLFPADSEHNKLKASQARDLLSKMLVID  
PAKRI SVDDALQHPYINVWYDPAEVEAPPPQIYDKQLDEREHTIEEWKELIYKEVMNSEEK  
TKNGVVKGQPSPSGAAVNSSES LPPSSSVNDISSMSTDQTLASDTDS SLEASAGPLGCCR

(SEQ ID NO:10)

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FIG. 5A

GGGGCTTGAGTGAGCTAAAGATTGGGTCTTCTTGAAATCACCTGTCTGTTATTATTTTAA  
 AACAAATCGCTACACCTCCAAAGACTCTGCTCCTTACTCCGGTTTGGAATGTGGCTAATGAC  
 TACCCAGTAGGGAGGATTTCTGGGGCAAACAGCCGACCAGGATCCTAGTTCTCAGGCACG  
 GAATGGCTATTGTGAGAACAGCACCAGCAGGATCATCGCAGATCTTGGTTATGGCCACTCA  
 GGCAAGACGCTGTTGAGTTAAGACCCCTTTCCCATAGATGAGAAGCCACAGAAGCAGTGGT  
 ATTTATGAGCCTCCATTTCTTATACTACTGCAGTGAACCAACCTTGGATGTGAAAATTGCC  
 TTTTGTGAGGGATTTCGATAAACACGTGGATGTGTCATCTATTGCCAAACATTACAACATGA  
 GCAAAAGCAAGGTGGACAACCAGTTCTACAGTGTGGAAGTGGGGGACTCAACCTTCACCGT  
 TCTTAAGCGCTACCAGAACCTGAAGCCAATTGGCTCTGGGGCTCAGGGAATAGTCTGTGCT  
 GCGTACGACGCTGTCCTTGACAGAAATGTGGCCATTAAGAAGCTCAGCAGACCCTTCCAGA  
 ACCAACTCACGCCAAGAGGGCTTACCGGGAGCTGGTGCTCATGAAGTGTGTGAACCATAA  
 AAACATTATTAGCTTATTAAATGTTTTTACACCCAGAAAACGCTGGAGGAGTTCCAAGAT  
 GTCTACTTAGTGATGGAACCTGATGGACGCCAACCTGTGTGAGGTGATTGAGATGGAGCTGG  
 ACCACGAGCGGATGTCTTACTTGCTGTACCAGATGCTGTGTGGCATCAAGCACCTCCACTC  
 CGCTGGGATCATCCACAGGGACTTAAAACCCAGTAACATTGTAGTCAAGTCTGATTGCACA  
 CTGAAAATCCTCGACTTCGGACTGGCCAGGACAGCGGGTACAAGCTTCATGATGACTCCGT  
 ATGTGGTGACGCGATATTACAGAGCCCCTGAGGTCATCCTGGGCATGGGCTACAAGGAGAA  
 CGTGGACATATGGTCTGTGGGATGCATCATGGGAGAAATGGTTCGCCACAAAATCCTCTTT  
 CCCGGAAGGAGCTATATTGACCAGTGGAACAAAGTCATCGAGCAGCTAGGAACTCCGTGTC  
 CAGAGTTCATGAAGAAATTGCAGCCACAGTCAGAACTACGTGGAGAATCGGCCCCAAGTA  
 CGCAGGACTCACCTTCCCCAAGCTCTTTCAGATTCCCTCTTCCAGCGGATTCTGAGCAC  
 AATAAACTTAAAGCCAGCCAAGCCAGGGATTTGTTGTCTAAGATGTTAGTGATTGACCCAG  
 TGAAGAGGATATCGGTGGACGACGCACTGCAGCATCCGTACATCAACGTTTGGTACGACCC  
 GGCTGAAGTGGAGGCGCCTCCGCCTCAGATATATGATAAGCAGCTGGATGAAAGGGAGCAC  
 ACCATCGAAGAATGGAAAGAACTTATCTACAAGGAGGTAATGAACTCAGAAGAGAAGACTA  
 AGAATGGCGTAGTCAAAAGCCAGCCCTCGCCTTCAGCACAGGTGCAGCAGTGAACAGCAGT  
 GAGAGTCTCCCTCCATCCTCGGCTGTCAACGACATCTCCTCCATGTCCACCGACCAGACCC  
 TCGCATCTGACACTGACAGCAGCCTGGAGGCCTCGGCGGGACCGTTGGGTTGTTGCAGGTG  
 ACTAGCCGCCTGCCTGCGAAACCCAGCGTTCTTCAGGAGATGACGCGATAGAACACAGCAC  
 ACATGCACACACACAGCTTGCTCTCACACACACTCAGCTTGCTCACACACACACACACA  
 TACACACAAACACACACTGTCTCTCTCTCACACACACACACTGTCACAACGCACTCACGAA  
 AGGTCAAGAAAAAATAACAATAGAGAGATCCAACATAAAATTAAGTTAAATTTTTCTGCG  
 TGCTTCTCCAAAGTTCTGTATCACAGCTGAGCTGAAATGTATACTTAACTTCTAGTTGCGC  
 TCGCTTTGGTTTCCCTCCAGCAGTGCTTACTACACAAGACAAATCAGACACAATTAGAGAA  
 ACCTTTCCCTAAAGTGTAAGTTAAGTGGCTGCAGAACCAGCAACCTGTAAGTGCCTTCAA  
 ATGGCATGAGGAGGTGGGCACGGGTCCCGCCCAGCATGTGTGTGTCTCTATCTCGCGTCTA  
 CCTGCTCTTCCGGCCTAGTCAGATGGATGTAGATACAGATCCCGCATGTGTCTGTATTCAA  
 ACAGCACTTAGAGATGCTCCTGTCAGTGTCTCCAGGCTCCACCAAGACACACACCGGGT  
 ACCACATGGTCCATTTTCATGTGATCTATTACTCTGACATAAATCCATCTGTAATATATTGC  
 CAGTATATAAGCTGTTTAGTTTGTAAATTGCTTAAGCTGTATGTCTTATAAGAGACTATGT  
 AAAGGGGGAAAATGGAGGCGTGAAGTCTCAGACCCTTGAAGATGTAGCTTCCGAATTTGAC  
 CGTTAAATGGCACCGTATACC (SEQ ID NO: 11)

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FIG. 5B

MSLHFLYYCSEPTLDVKIAFCQGFDKHVDVSSI AKHYNMSKSKVDNQFY SVEVG DSTFTVL  
KRYQNLKPIGSGAQGIVCAAYDAVLDNRNVAIKKLSRPFQNO THAKRAYREL VLMKCVNHKN  
IISLLNVFTPQKTLEEFQDVYLVME LMDANLCQVIQMEL DHERMSYLLYQMLCGIKHLHSA  
GIIHRDLKPSNIVVKS DCTLKILDFGLARTAGTSFM MTPYVVTRY YRAPEVILGMGYKENV  
DIWSVGCIMGEMVRHKILFPGRSYIDQWNKVIEQLGTPCPEFMKKLQPTVRNYVENRPKYA  
GLTFPKLFPDSLFPADSEHNKLKASQARDLLSKMLVIDPVKRISVDDALQHPYINVWYDPA  
EVEAPPPQIYDKQLDEREHTIEEWKELIYKEVMNSEEKTNGVVKSQPSPSAQVQQ (seq ID NO: 12)

362007 " 2252750

FIG. 6

JNK3 GENE LOCUS AND  
TARGETING VECTOR

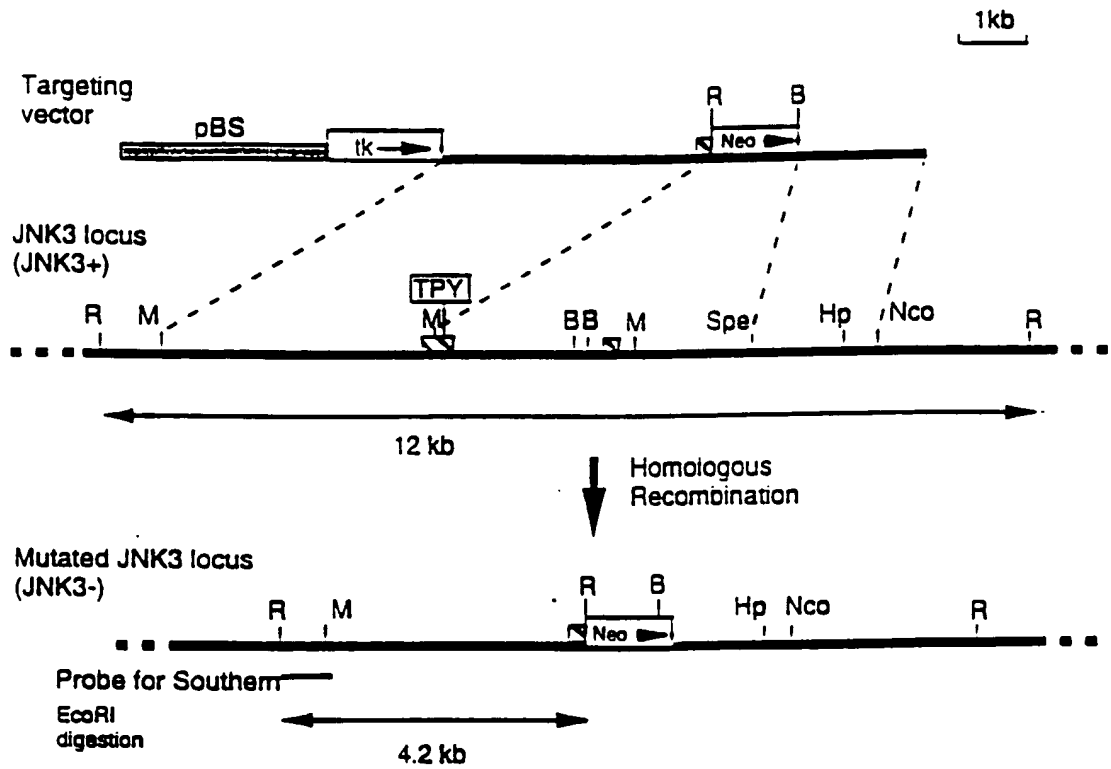


FIG. 7

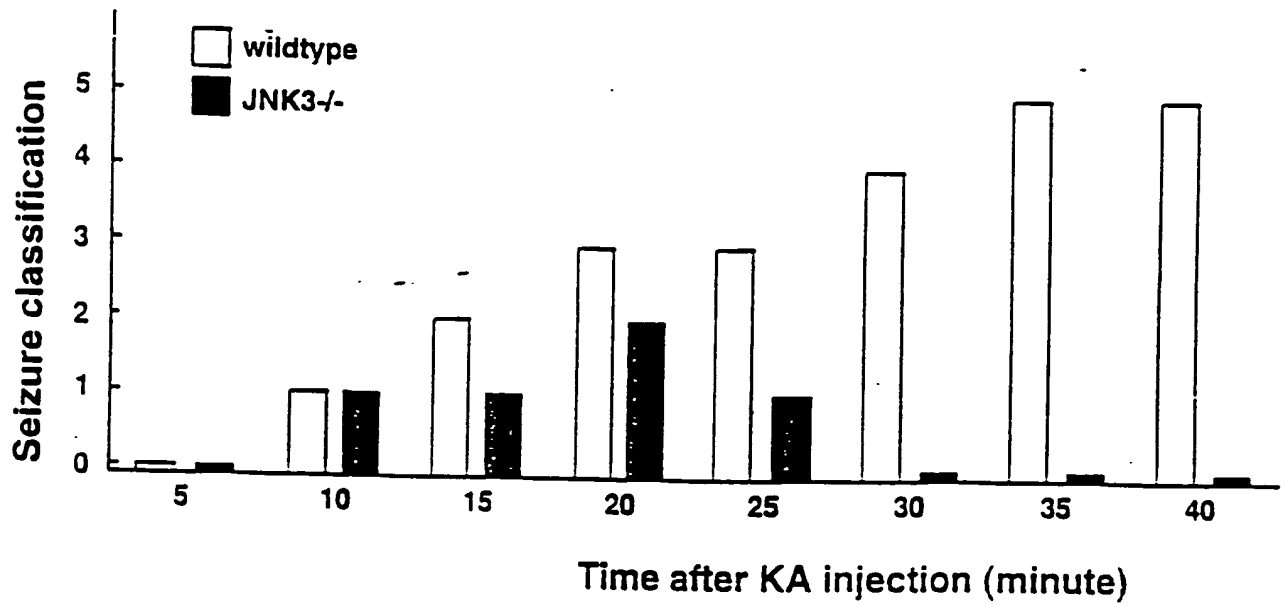


FIG. 8

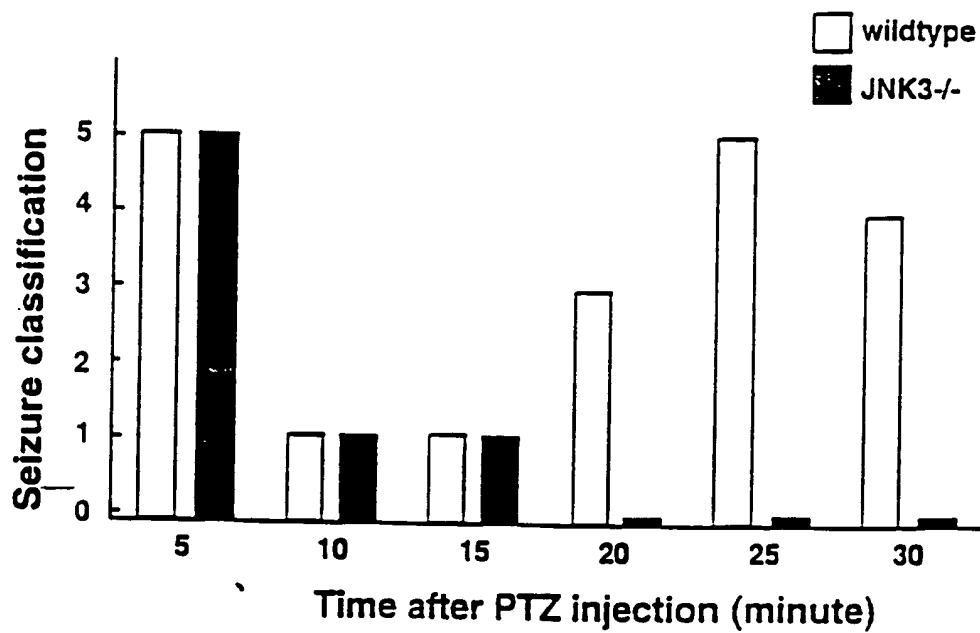




Fig. 9A

agcaactttc ctgacccaga ggaccggttaa caagtggccg ggagcaactt ttgcaaactc  
 cttctgcgcc ttaaggctgc caccgagact gtaaagaaaa ggagaagagg aacctatact  
 cataccagtt cgcacaggcc taagttgggc gaggcctagc cgcggctgcc tagcgtcccc  
 cccccctca cagcggagga ggggacagtt gttggaggcc gggcggcaga cccgatcgcg  
 ggccctccacc gagaattccg tgacgactgg tcagcaccgc cggagagccg ctgttgctgg  
 gactggtctg cgggctccaa ggaaccgctg ctccccgaga gcgctccgtg agtgaccgcg  
 acttttcaaa gctcggcatc gcgcggagtc ctaccaacgt gagtgctagc ggagtcttaa  
 ccctgcgctc cctggagcga actggggagg agggctcagg ggggaagcact gccgtctgga  
 gcgcacgctc taaacaaact ttgttacaga agcaggagcg cgcgggtatc cccccgcttc  
 ccggcgcgct gttgcggccc cgaaacttct gcgcacagcc caggctaacc ccgctgaag  
 tgacggaccg ttctatgact gcaaagatgg aaacgacctt ctacgacgat gccctcaacg  
 cctcgcttct ccagtcgag agcgggtgct acggctacag taaccctaag atcctaaaac  
 agagcatgac cttgaacctg gccgaccggt tgggcagtct gaagccgcac ctccgcgcca  
 agaactcgga ctttctcacg tcgcccagcg tcgggctgct caagctggcg tcgccggagc  
 tggagcgctt gatcatccag tccagcaatg ggcacatcac cactacaccg acccccaccc  
 agttcttgtg cccaagaac gtgaccgacg agcaggaggg cttcgccgag ggcttcgtgc  
 gcgccctggc tgaactgcat agccagaaca cgcttcccag tgtcacctcc gcggcacagc  
 cggtcagcgg ggcgggcatg gtggctcccg cggtggcctc agtagcaggc gctggcgggc  
 gtgggtggcta cagcgccagc ctgcacagtg agcctccggt ctacgccaac ctcagcaact  
 tcaaccgggg tgcgctgagc agcggcggtg gggcgccctc ctatggcgcg gccgggctgg  
 cctttccctc gcagccgcag cagcagcagc agccgcctca gccgcgcac cacttgcccc  
 aacagatccc ggtgcagcac ccgcggctgc aagccctgaa ggaagagccg cagaccgtgc  
 cggagatgcc gggagagacg ccgcccctgt cccctatcga catggagtct caggagcgga  
 tcaaggcaga gaggaagcgc atgaggaacc gcattgccgc ctccaagtgc cggaaaagga  
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 aacagactgt cagggctgag gggcaatgga agaaaaaaa taacagagac aaacttgaga  
 acttgactgg ttgcgacaga gaaaaaaaaa gtgtccgagt actgaagcca agggtaaca  
 agatggactg ggttcggact gacggcgccc ccagtgtgct ctggagtggg aaggacgtgg  
 cgcgcctggc tttggcgtgg agccagagag caggcctatt ggccggcaga ctttgcggag  
 cgctgtgccg cgcgcgacca gaacgatgga cttttcgtaa acattgacca agaactgcat  
 ggacctaaca ttcgatctca ttcagtatta aaggggggtg ggaggggtta caaactgcaa  
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 gggggaggct tgtaagtgcc aggctagact gcagatgaac tcccctggcc tgcctctctc  
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 acagcttctt gcctttgtaa gttattccat gtttgtttgt ttgggtgtcc tgcccagtgt  
 ttgtaaataa gagatttgaa gcattctgag tttaccattt gtaataaagt atataatttt  
 tttatgtttt gtttctgaaa atttccagaa aggatattta agaaaatata ataaactatt  
 gaaaagt (SEQ ID NO:13)

Fig. 9B

MTAKMETTFYDDALNASFLQSESGAYGYSNPKILKQSMTLNLAD  
PVGSLKPHLRAKNSDLLTSPDVGLLKLASPELERLI IQSSNGHITTTPTPTQFLCPKN  
VTDEQEGFAEGFVRALAEHSQNTLPSVTSAAQPVSGAGMVAPAVASVAGAGGGGGYS  
ASLHSEPPVYANLSNFNPGALSSGGGAPSYGAAGLAFPSQPQQQQQPPQPPHHLPPQI  
PVQHPRLQALKEEPQTVPEMPGETPPLSPIDMESQERIKAEKRMRNRRIAASKCRKRK  
LERIARLEEKVKTLKAQNSELASTANMLREQVAQLKQKVMNHVNSGCQLMLTQQLQTF  
(SEQ ID NO:14)

[illegible]

Fig. 10A

ataccagaga	ctcaaaaaaa	aaaaaaaagt	tccagattgc	tggacaatga	cccgggtctc
atcccttgac	cctgggaacc	gggtccacat	tgaatcaggt	gcgaatgttc	gctcgccttc
tctgcctttc	ccgcctcccc	tcccccgcc	gcggcccccg	ttccccccct	gcgctgcacc
ctcagagttg	gctgcagccg	gcgagctggt	cccgtcaatc	cctccctcct	ttacacagga
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gggggaccat	ctccgaaatc	ctacacgcgg	aaggtctagg	agaccccccta	agatcccaaa
tgtgaacact	cataggtgaa	agatgtatgc	caagacgggg	gttgaaagcc	tggggcgtag
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gcccagtgac	gtaggaagtc	catccattca	cagcgcttct	ataaaggcgc	cagctgaggc
gcctactact	ccaaccgcga	ctgcagcgag	caactgagaa	gactggatag	agccggcggt
tccgcgaacg	agcagtgacc	gcgctcccac	ccagctctgc	tctgcagctc	ccaccagtgt
ctacccctgg	accccttgcc	gggctttccc	caaacttcga	ccatgatgtt	ctcgggtttc
aacgccgact	acgaggcgtc	atcctcccg	tgcagtagcg	cctccccggc	cggggacagc
ctttcctact	accattcccc	agccgaactc	ttctccagca	tgggctctcc	tgtcaacaca
caggtgagtt	tggctttgtg	tagccgccag	gtccgcgctg	agggtcgccg	tggaggagac
actgggggtg	gactcgcagg	ggcggggggg	tcttcctttt	tgcgtctgga	gggagactgg
cgcggtcaga	gcagccttag	cctgggaacc	caggacttgt	ctgagcgcgt	gcacacttgt
catagtaaga	cttagtgacc	ccttcccgcg	cggcagggtt	attctgagtg	gcctgcctgc
attcttctct	cggccgactt	gtttctgaga	tcagccgggg	ccaacaagtc	tcgagcaaag
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accttaactg	aatgtttggtc	cttttcttct	atagctatct	cctgaagagg	aagagaaacg
gagaatccga	agggaaacga	ataagatggc	tgcagccaag	tgccggaatc	ggaggaggga
gctgacagat	acactccaag	cggtagggtg	aaccagctgc	tgctcctgaa	actttattaa
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tgagattgcc	aatctgctga	aagagaagga	aaaactggag	tttatttttg	cagcccaccg
acctgctctg	aagatccccg	atgaccttgg	cttcccagag	gagatgtctg	tggcctccct
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gccccctctc	aacgaccctg	agcccaagcc	atccttggag	ccagtcaaga	gcatacagca
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agactgggag	cctctgcaca	gcaattcctt	ggggatgggg	cccatggtca	cagagctgga
gccccctgtg	actcccgtgg	tcacctgtac	tccgggctgc	actacttaca	cgtcttccct
tgtcttcacc	taccctgaag	ctgactcctt	cccaagctgt	gccgctgccc	accgaaaggg
cagcagcagc	aacgagccct	cctccgactc	cctgagctca	cccacgctgc	tggccctgtg

Fig. 10B

agcagtcaga gaaggcaagg cagccggcat ccagacgtgc cactgcccga gctgggtgcat  
tacagagagg agaaacacgt cttccctcga aggttcccgt cgacctaggg aggaccttac  
ctgttcgtga aacacaccag gctgtgggcc tcaaggactt gcaagcatcc acatctggcc  
tccagtcctc acctcttcca gagatgtagc aaaaacaaaa caaaaaccg  
catggagtgt gttgttccta gtgacacctg agagctggta gttagtagag catgtgagtc  
aaggcctggg ctgtgtctct tttctcttct tccttagttt tctcatagca ctaactaatc  
tggtgggttc attattggaa ttaacctggg gctggattgt atctagtgc gctgatttta  
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taagaaaaga taggacttta ttttccagta gatagaaatc aatagctata tccatgtact  
gtagtccttc agcgtcaatg ttcattgtca tgttactgat catgcattgt cgagggtggc  
tgaatgttct gacattaaca gttttccatg aaaacgtttt tattgtgttt tcaatttatt  
tattaagatg gattctcaga tatttatatt tttattttat ttttttctac cctgaggtct  
ttcgacatgt ggaaagtga tttgaatgaa aaattttaag cattgtttgc ttattgttcc  
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FIG. 11

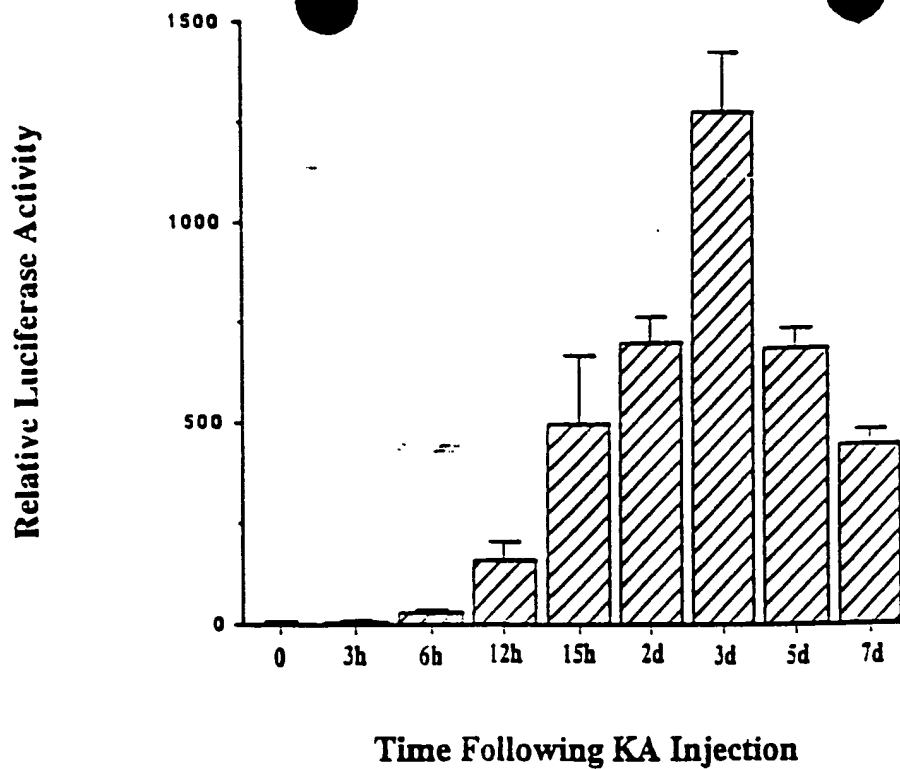


FIG. 12

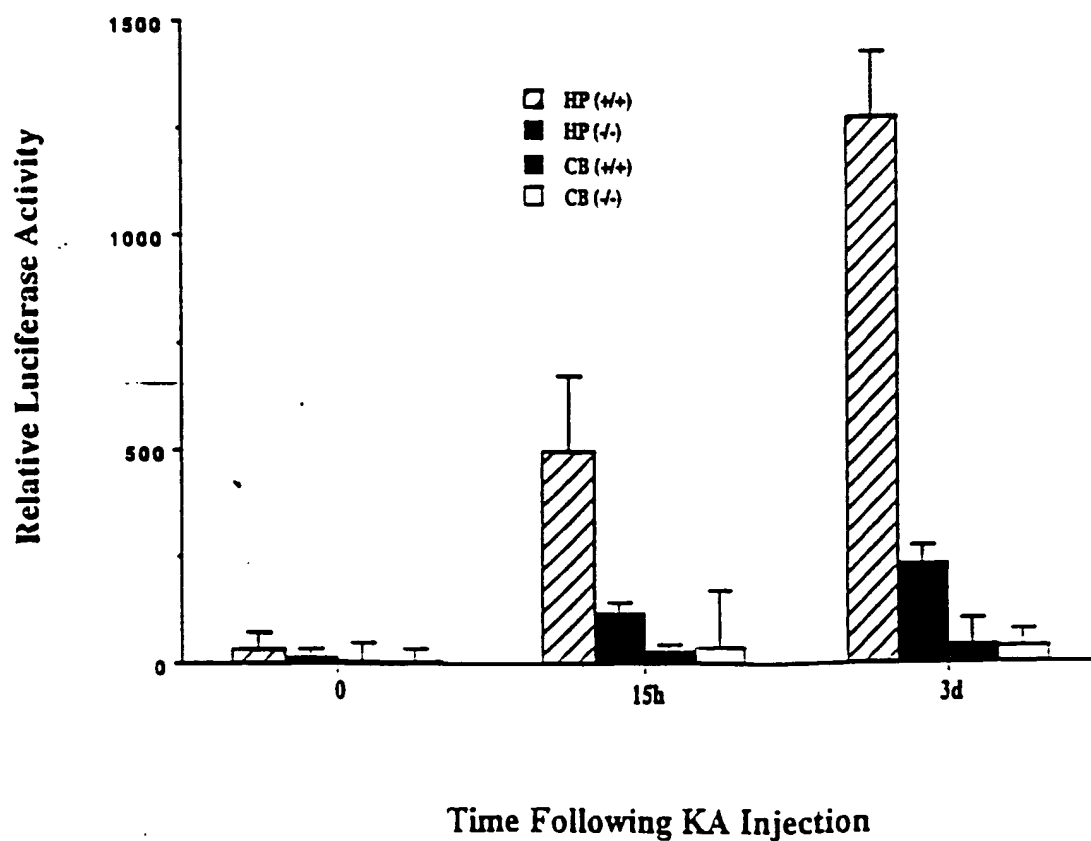


FIG. 13

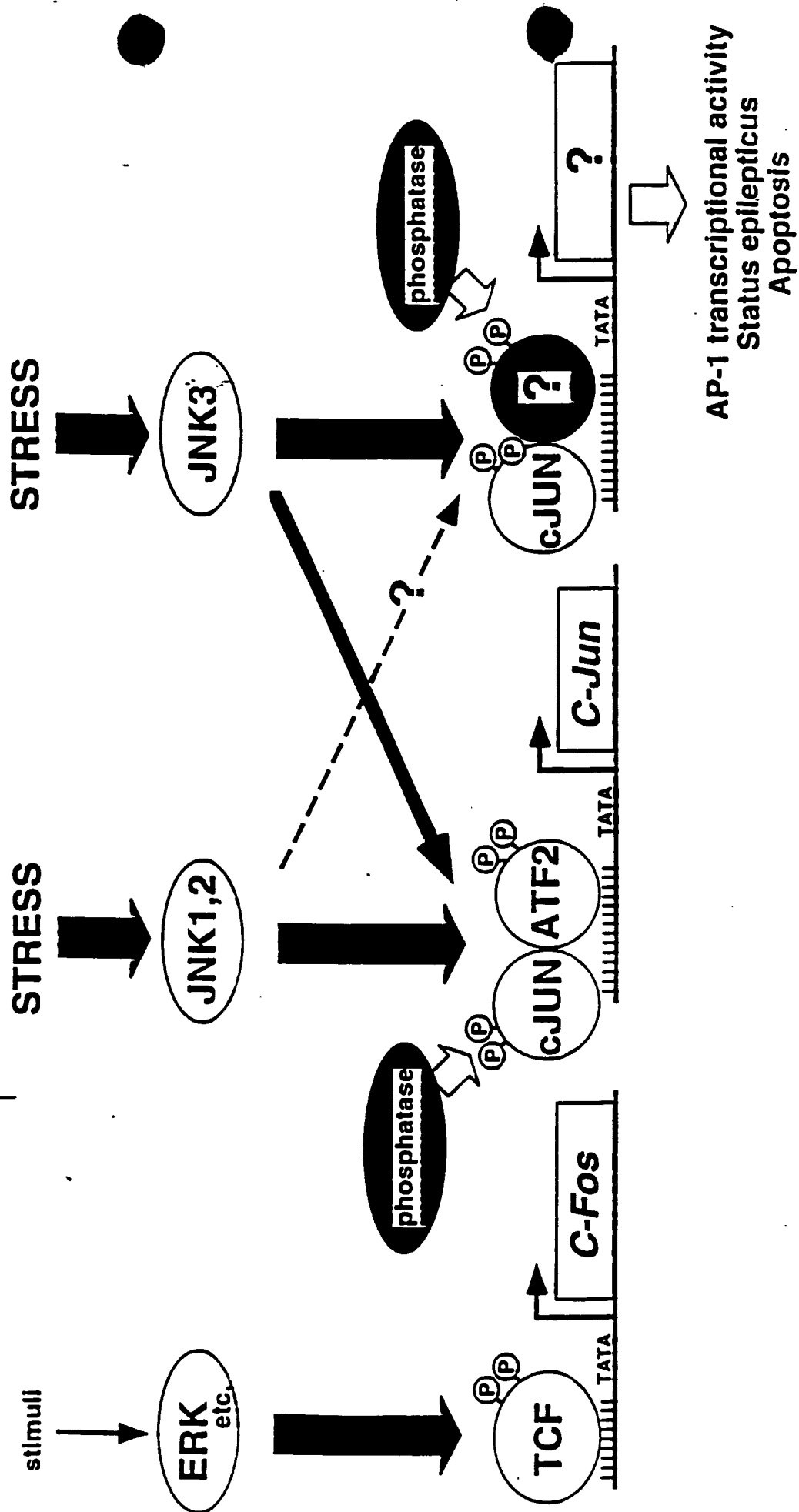


FIG. 14

